75 mg/m^2 with GVHD prophylaxis of cyclosporin (CSA) and mycophenolate (MMF). The median nucleated cell (NC) dose was 3.5×10^7/kg, 60% were 4/6 HLA mismatched. Sustained donor engraftment was seen in 88% (95% CI: 83-97) at a median of 24 days. Complete donor chimerism was derived from one unit by day 60 in all but 4 patients. The incidence of grade III-IV acute GVHD was 17% and chronic GVHD was 20%; TRM at 6 months was 22%. With a median follow-up of 20 months, 2 yr survival and DFS was 63% and 59%. 93 patients (median age: 52 years (range: 17-69) who were aged >45 or had preexisting co-morbidities received non-myeloablative conditioning with CY 50 mg/kg, FLU 200 mg/m^2/day and TBI 200 cGy followed by double UCBT. GVHD prophylaxis also consisted of CSA and MMF. The median NC dose was 3.7×10^7/kg with 61% having at least one 4/6 HLA mismatched unit. Sustained donor engraftment was seen in 83% at a median of 12 days with donor chimerism >90% by day 100. The incidence of grade III-IV acute GVHD, CGVHD and TRM was 23%, 22%, and 15%, respectively. Probability of DFS at 2 years is 49% (95% CI: 38-60) with a median follow up of 19 months. These results indicate that the co-infusion of two partially HLA matched UCB units after myeloablative or non-myeloablative conditioning results in a high incidence of engraftment, and low rates of AGVHD, CGVHD and TRM. Randomized trials are required to determine the relative benefit of double UCBT as compared to single UCBT or transplantation of HLA matched marrow.

5

DOUBLE CORD BLOOD TRANSPLANTATION IN ADULTS USING A REDUCED INTENSITY CHEMOTHERAPY ONLY CONDITIONING REGIMEN

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Umbilical cord blood is a useful stem cell source for patients without matched donors. Adult cord blood transplantation is limited by the low cell dose in most individual cord blood units. Initial studies using single cord blood units with a myeloablative conditioning regimen reported a 100 day transplant related mortality of over 40%. Double cord blood transplantation (two units administered sequentially) provides a higher cell dose, and a reduced intensity conditioning regimen may decrease transplant related mortality.

We have treated 35 patients with this approach using a conditioning regimen of fludarabine 30 mg/m^2/day days −8 through −3 (total dose 180 mg/m^2), melphalan 100 mg/m^2 day −2 and rabbit antithymocyte globulin 1.5 mg/kg days −7, −5, −3, −1 (total dose 6 mg/kg). Cord blood units were a 4/6 or higher HLA A, B, DR allele match with the patient and each other and achieved a minimum precryopreservation cell dose of 3.7×10^7 NC/kg. Twenty one patients received GVHD prophylaxis with cyclosporine and mycophenolate mofetil and fourteen patients received GVHD prophylaxis with tacrolimus and sirolimus. Only five patients treated with sirolimus and tacrolimus have greater than 100 days of follow up; the results with this GVHD regimen will be reported subsequently.

For the cyclosporine/mycophenolate mofetil patients the median days to neutrophil and platelet engraftment (platelet count greater than 20,000 unsupported) were 20 and 41 days respectively. Fifteen of 21 patients are alive with a median follow up of 16 months. One patient with CLL has progressive disease. The 100 day transplant related mortality is 14%, with the deaths from post-transplant lymphoproliferative disorder, central nervous system bleeding, and staphylococcal sepsis. One year disease free survival is 66%. Double cord blood transplantation with a reduced intensity regimen may be a safer option for patients requiring cord blood transplantation.

6

RISK OF RELAPSE AFTER UMBILICAL CORD BLOOD TRANSPLANTATION IN PATIENTS WITH ACUTE LEUKEMIA: MARKED REDUCTION IN RECIPIENTS OF TWO UNITS

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We analyzed patients with acute leukemia transplanted with myeloablative conditioning at a single institution to determine if there were any unique risk factors associated with relapse after UCBT. Ninety-six consecutive patients were evaluated, 39 were >18 years of age, 50 were male; 46 were CMV seropositive; 50 had ALL and 46 had AML. Two different conditioning regimens were used. Regimen A consisted of cyclophosphamide 120 mg/kg, TBI 1320-1375 cGy, and ATG, followed by cyclosporine A (CSA)/methylprednisolone immunosuppression (n = 53). Regimen B consisted of cyclophosphamide 120 mg/kg, fludarabine 75 mg/m^2, TBI 1320-1375 cGy pre-transplant and CSA/mycophenolate mofetil immunosuppression (n = 43). Patients received either one (n = 67) or two (n = 29) 4-6/6 HLA-matched UCB units, so that the total IVCNC count was $>2.5 \times 10^7$/kg. Accordingly, the demographics for recipients of one or two UCB units were similar except for older age (median age 24 vs 8, $P < 0.01$) and greater weight (median 70 vs 32 kg, $P < 0.01$) for recipients of two UCB units. Potential risk factors for relapse that were evaluated included: age, gender, recipient CMV sero-status, diagnosis, disease risk, HLA disparity, regimen (A vs B), and TNC (or CD34$^+$) dose of the unit responsible for sustained engraftment.

Notably, in Cox regression analysis two factors were associated with lower relapse risk: disease risk (CR1/CR2 vs CR3+/REL [RR 0.32, $P = 0.02$]) and transplantation of two UCB units (RR 0.3, $P = 0.03$). Importantly, the diagnosis, UCB graft cell dose, and presence of acute GVHD had no demonstrable impact. All recipients of regimen A received a single UCB unit (relapse was 28% (95% CI, 15-41%)), thus interactions between regimen A and number of UCB units could not be assessed. Patients who received regimen B in CR1/2, showed a significantly lower risk of relapse with two UCB units compared to one unit (11% vs 54%, $P < 0.01$). No significant difference in relapse risk could be discerned for patients with advanced disease (CR3-REL) when comparing single vs double UCBT ($P = 0.48$).

This report is the first suggesting that double unit UCB grafts may be associated with reduced relapse risk in acute leukemia. Larger studies are needed to confirm this clinical experience and to investigate the potential mechanisms by which double unit grafts could mediate protection against relapse.

7

MYELOABLATIVE SINGLE CORD TRANSPLANTS (SCT) VERSUS DUAL CORD TRANSPLANTS (DCT) IN ADULTS WITH ACUTE LEUKEMIA

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Background: Combining 2 cord blood products overcomes the total nucleated cell (TNC) dose limitation and may improve clinical outcomes following allogeneic cord blood (CB) transplantation in adults. We performed a retrospective case-control study in adult patients with acute leukemia receiving myeloablative conditioning and 1 or 2 cord blood units to identify potential causes for differences in clinical outcomes following SCT and DCT and product characteristics predictive of long-term engraftment in DCT recipients.

Study design: To evaluate 20 DCT cases, we selected 20 SCT with the largest TNC dose as controls from a cohort of 103 adult SCT patients. SCT and DCT were matched for age, sex, diagnosis, disease status, ethnicity and body weight ($0.11 \leq P \leq 0.78$) excluding patients with graft failure or previous transplants.

Results: Administered TNC dose for DCT (3.7×10^7/kg) was nearly 2-fold greater than SCT (1.9×10^7/kg, $P < 0.0001$) with no significant differences in post-thaw TNC recovery ($P = 0.13$). Time to ANC >500/uL for DCT was 17 days compared to 20 days for SCT ($P < 0.02$). For SCT, there were 9 and 11 patients with 1 or 2 Ag mismatch at HLA-A,B or DRB1, respectively, (mean = 1.6 Ag mismatch). Three-way comparison of both donors and recipient for DCT also gave mean = 1.6 Ag mismatch. Overall survival (OS) at 12 months was 18% for SCT and 72% for DCT ($P < 0.0001$) with median duration of follow-up of >18 months for both SCT and DCT. OS was significantly correlated with post-thaw TNC dose for SCT ($P < 0.04$) but not for DCT ($P = 0.88$). In the first 100 days post-transplant, infection rates for SCT (65%)